Remarks

Claims 80-107 are pending in the subject application. Applicants acknowledge that claims 86, 96-99 and 103 have been withdrawn from further consideration as being drawn to a non-elected invention. By this Amendment, Applicants have canceled claim 100, amended claims 80, 101 and 104 and added new claims 108-110. Support for the amendments and new claims can be found throughout the subject specification and in the claims as originally filed (see, for example, paragraphs 35 and 158). Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 80-99 and 101-110 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

Claims 80-88, 90-95 and 102 are rejected under 35 U.S.C. § 103(a) as obvious over BioNews (2002) in view of Espinosa *et al.* (2001). Applicants respectfully assert that the claimed invention is not obvious over the cited references and traverse the rejection of record. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) is respectfully requested.

In rejecting the claimed invention, the Office Action argues that BioNews teaches the treatment of renal cell carcinoma patients via the administration of Phosphstim (an activator of gamma delta T-cells). The Office Action admits that BioNews does not teach the use of a pharmaceutical acceptable carrier and the amounts of Phosphostim to be administered to the patient in order to induce an increase in the gamma-delta T cell population in the subject having renal carcinoma. However, in an effort to remedy the defects in the purported teachings of the BioNews press release, the Office Action relies on Espinosa *et al.* to teach a composition comprising BrHPP (Phosphostim) in water (*i.e.*, a pharmaceutically acceptable carrier, see page 18338, last three lines of the first paragraph of left column). Espinosa *et al.* further teach that a solution of BrHPP increases the gamma-delta T cell population among total T cells in culture up to 20% at 12.5 nanomolar, 30% at 25 nanomolar and 50% at 100 nanomolar. Thus, the Office Action argues, it would have been *prima facie* obvious for a person of ordinary skill in the art to treat patients with renal carcinoma comprising the administration of Phosphostim (BrHPP) as taught by BioNews, and further comprising a pharmaceutically acceptable carrier as taught by Espinosa *et al.*, with the motivation of better delivering the active ingredient Phosphostim (BrHPP) to the patient. It would be further obvious to adjust the amount of Phosphostim (BrHPP) to be administered to the patient in order to

increase the activity of gamma-delta T cells *in vivo*, based in the amounts disclosed by Espinosa *et al. in vitro*, since the person skilled in the art will be able to extrapolate *in vitro* data into *in vivo* data and further determine the specific amount of Phosphostim to be administered to a particular patient and adjust the dosage amounts based on the observed clinical effectiveness and the amount of increase in the gamma-delta T cell population, thus resulting in the practice of claims 80-81, 86-88, 90-93 and 102 with a reasonable expectation of success.

Applicants submit that the newly amended claims are not rendered obvious by the combined teachings of BioNews in view of Espinosa *et al.* Particularly, the cited combination of references fails to teach all the limitations of the presently claimed invention. As the Patent Office is aware, an obviousness rejection fails if the prior art relied on does not disclose all of the limitations of the claimed invention. *See, e.g., In re Zurko*, 258 F.3d 1379, 1385-86 (Fed. Cir. 2001). Thus, obviousness requires a teaching or suggestion of all limitations in a claim. *CFMT, Inc. v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) (citing *In re Royka*, 490 F.2d 981, 985 (C.C.P.A. 1974)). Accordingly reconsideration and withdrawal of the rejection is respectfully requested.

Claims 100-101 and 104-107 are rejected under 35 U.S.C. § 103(a) as obvious over BioNews (2002) in view of Espinosa *et al.* (2001) and in further view of Negrier *et al.* (1998). Applicants respectfully assert that the claimed invention is not obvious over the cited references.

The Office Action argues that BioNews in view of Espinosa *et al.* teach all the limitations of claim 100, except for the administration of an interleukin-2 polypeptide. However, Negrier *et al.* teach that interleukin-2 induces notable tumor regression in a limited number of patients with metastatic renal-cell carcinoma. The Office Action further argues that, at the time of the invention, it would have been *prima facie* obvious for a person of ordinary skill in the art to treat renal cancer combining two compositions (Phosphostim and Interleukin-2) each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art. The Office Action further argues that, for claim claims 101 and 104-107, Negrier *et al.* further teach that interleukin-2 was administered as a five-day continuous intravenous infusion at a dose of 18×10^6 IU per square meter of body surface area per day and that while Negrier *et al.* do not teach the exact amounts and dose regimen disclosed in claims 101 and 104-107, it is within the

capability of the ordinary artisan to adjust the dose regimen based on the observed clinical effectiveness, thus resulting in the practice of claims 101 and 104-107 with a reasonable expectation of success. Applicants respectfully disagree.

To the extent that the examiner argues that the combination of BioNews (2002), Espinosa *et al.* (2001) and Negrier *et al.* (1998) renders the claims obvious because it would naturally follow from these references that one could treat renal cell carcinoma using the separate teachings of the references, Applicants note that IL-2 and stimulated gamma delta T-cells generate their respective effects on renal cell carcinoma in substantially different manners. Even if these methods may both be classified as methods for treating renal cell carcinoma, the rejection does not demonstrate that one of ordinary skill in the art would regard both as useful for the same purpose and functioning in the same manner (e.g., cytokine therapy versus cell mediated cytotoxicity). Applicants also submit that there is no evidence of record that suggests that these two diverse treatment regimens would be useful in combination for the treatment of renal cell carcinoma, particularly since Negrier *et al.* indicate that none of the three tested cytokine therapies demonstrated any advantage in survival for the treated patients (see page 1277, column 2, last paragraph).

Even assuming that this is the case, Applicants further submit that there is no rationale provided as to why one skilled in the art would have been motivated to use low dose IL-2 for the treatment of renal cell carcinoma. In this respect, Negrier *et al.* teach the use of 18×10^6 IU (18 MU) of IL-2 for the treatment of renal cell carcinoma. Other than the assertion made in the Office Action, no reasoning is provided as to why one skilled in the art would have been motivated to use low dose IL-2 therapy (*e.g.*, ranging from 0.2-2 MU IL-2) for the treatment of renal cell carcinoma. As the Supreme Court stated, "*there must be some articulated reasoning* with some rational underpinning to support the legal conclusion of obviousness." *KSR Int'l v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006) (emphasis added)). In this case, no such articulated reasoning is provided (other than the argument that "it is within the capability of the ordinary artisan to adjust the dose regimen based on the observed clinical effectiveness"; Office Action at page 10). Applicants submit that the ordinary artisan would not have been motivated to use IL-2 doses that are between 9 and 90 times lower than that taught in Negrier *et al.* Accordingly, it is respectfully submitted that a *prima facie case* of obviousness has not been established and

reconsideration and withdrawal of the rejection is respectfully requested.

Applicants further request the courtesy of an interview in this matter at such time as the Examiner considers this response.

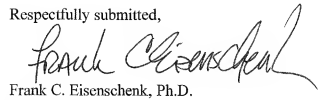
It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position. Applicants expressly reserve the right to pursue the invention(s) disclosed in the subject application, including any subject matter canceled or not pursued during prosecution of the subject application, in a related application.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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